Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

EFNS task force: the use of neuroimaging in the diagnosis of dementia.

Bibliographic Source(s)

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

The levels of evidence (class I-IV) supporting the recommendations and ratings of recommendations (A-C, Good Practice Point) are defined at the end of the "Major Recommendations" field.

Recommendations for Structural Magnetic Resonance Imaging (MRI)

1. Structural imaging should be carried out at least once in the diagnostic work-up of patients with cognitive impairment and serves at least three purposes: to exclude other potentially treatable diseases, to recognize vascular lesions and to identify specific findings to help distinguish different forms of neurodegenerative types of dementia (Good Practice Point).
2. MRI is currently the imaging modality of choice for assessing subjects with suspected dementia. However, where MRI is not available or contraindicated, computed tomography (CT) scans can usefully exclude major space occupying lesions, large infarcts and hydrocephalus (Good Practice Point). Multi-detector row CT is the best alternative for patients who cannot undergo MRI (Good Practice Point).
3. A standard MRI protocol should include a high-resolution structural volumetric T1-weighted scan, transverse T2-weighted and fluid attenuated inversion recovery (FLAIR) sequences and transverse T2*-gradient echo sequence (Good Practice Point). Routine contrast administration is not indicated (Good Practice Point). Diffusion-weighted imaging (DWI) can be useful to identify recent infarcts, as well as cortical and/or basal ganglia changes in Creutzfeldt-Jakob disease (CJD) patients (Good Practice Point).
4. It is particularly difficult to attribute clinical significance to evidence of cerebrovascular disease in patients with cognitive impairment. Vascular changes on CT or MRI do not preclude a diagnosis of degenerative dementia, especially in older age. A diagnosis of vascular dementia should only be made where the vascular lesion(s) can explain the cognitive deficit (Class II, Level A). The 'mixed dementia' label should be reserved for those cases in which both clinical features and diagnostic markers point to a mixed aetiology (Good Practice Point).
5. T1-weighted images should be carefully evaluated to assess specific patterns of focal atrophy, especially in the medial temporal lobes (MTL), biparietal regions and posterior cingulate cortex (as seen in Alzheimer's disease [AD]), temporal pole and/or frontal lobes (as seen

in frontotemporal dementia [FTD]), parietal/occipital lobe (as seen in posterior cortical atrophy [PCA]), putamen, and midbrain and frontal lobe (as seen in progressive supranuclear palsy [PSP]) (Good Practice Point).

6. Coronal T1-weighted sequence can be used to assess MTL atrophy to support a clinical diagnosis of AD compared with cognitively normal subjects (Class II, Level A). Prediction of subsequent AD in individuals with amnestic mild cognitive impairment (MCI) can also be obtained with MRI volumetric measures of the MTL (Class II, Level A). However, at present, accepted standards for quantitative MTL volume measurement are lacking. Therefore, quantification must rely on local specific standards (Good Practice Point).

7. Combining MTL measures with other potentially informative markers, such as posterior cingulate cortex and precuneus volumetric measures, are likely to improve diagnostic confidence in AD patients (Class II, Level B), mainly in younger cases.

8. In cases of atypical AD presentations, the involvement of the MTL is reported less consistently than that of lateral temporal and medial parietal regions (Class III, Level B).

9. No established structural MRI pattern is characteristic for dementia with Lewy bodies (DLB) (Class II, Level A). However, the absence of MTL atrophy on CT or MRI may be suggestive of a diagnosis of DLB compared with AD (Class II, Level A).

10. The pattern of atrophy is more useful than atrophy of single regions in the differential diagnosis of FTD compared with AD: knife-edge, severe frontotemporal atrophy combined with dilatation of frontal horn, and an anterior greater than posterior gradient is suggestive of a diagnosis of FTD (Class II, Level A).

11. A normal structural MRI scan should prompt the clinician to reconsider a diagnosis of behavioural variant of frontotemporal dementia (bvFTD), if clinically severe, and semantic variant primary progressive aphasia (PPA) (Good Practice Point).

12. Presence of knife-edge frontal and/or temporal lobe atrophy in patients with PPA is predictive of FTLD pathology, whilst the presence of temporoparietal atrophy is highly associated with AD (Class III, Level C).

Recommendations for Functional Imaging

1. Although typical cases of dementia may not benefit from routine single positron emission computed tomography (SPECT) or positron emission tomography (PET) imaging, these tools are recommended in those cases where diagnosis remains in doubt after clinical and structural MRI work-up and in particular clinical settings (Class II, Level A).

2. Functional imaging can be of value to diagnose (or exclude) a neurodegenerative dementia in those subjects with cognitive impairment presenting with severe psychiatric disturbances (including depression and agitation) and in cases where proper cognitive testing is difficult, that is, with no language in common with the clinician (Good Practice Point).

3. Normal fluorine-18 (^{18}F)-2-fluoro-2-deoxy-D-glucose (FDG) PET scan findings, in the presence of the suspicion of dementia, make a neurodegenerative diagnosis less likely (Class II, Level A).

4. The overall regional pattern of metabolic impairment of the posterior cingulate/precuneus and lateral temporoparietal cortices, more accentuated than frontal cortex deficits, together with the relative preservation of the primary sensorimotor and visual cortices, basal ganglia and cerebellum defines the distinct metabolic phenotype of AD (Class II, Level A).

5. AD-like metabolic patterns in patients with MCI are predictive of conversion to AD within several years (Class II, Level A).

6. Occipital hypometabolism, particularly in the primary visual cortex, may be more common in DLB than AD on a group basis (Class II, Level B). However, on individual scans, the appearances of DLB and AD can be identical. Moreover, occipital hypometabolism is not a specific marker for DLB and can be associated with AD (Good Practice Point).

7. Although an overlap of functional abnormalities between FTD and AD has been shown to occur, the presence of posterior temporal and parietal brain hypoperfusion or hypometabolism is predictive of a pathological diagnosis of AD, whereas a disproportionate reduction in frontal perfusion/metabolism is more common in FTD cases (Class II, Level A).

8. In PPA patients, bilateral posterior temporoparietal hypometabolism (PET) or hypoperfusion (SPECT) is predictive of AD pathology; normal bilateral posterior temporoparietal function is specific for FTLD (Class III, Level C).

9. Dopaminergic SPECT is useful to distinguish DLB from AD (Class I, Level A), especially when there are no clear extrapyramidal symptoms and signs. However, a negative ^{123}I-2beta-carbometoxy-3beta-(4-iodophenyl)-N-(3-fluoropropyl) nortropane (^{123}I-FP-CIT) scan does not necessarily exclude a diagnosis of probable DLB, as around 20% of individuals with probable DLB appear to have normal scans (Class I, Level A).

10. Dopaminergic SPECT can be useful in differentiating DLB from long-term psychiatric patients on neuroleptic drugs, whose parkinsonism may be drug-induced (Good Practice Point).

Recommendations for Amyloid Imaging

1. Amyloid imaging is not yet recommended for routine use in the clinical setting, especially in the diagnostic work-up of patients with straightforward clinical AD as these patients are very likely to have positive scans (Class III, Level B).

2. Negative amyloid scans indicate absence of AD pathology with a high level of accuracy (Class III, Level B), but healthy elderly controls might have positive amyloid scans, so their predictive value in isolation is not clear (Good Practice Point).

3. Amyloid imaging is likely to find clinical utility in the following fields:
    i. The stratification of MCI patients into those with and without underlying AD (Class III, Level B)
    ii. The evaluation of early-onset AD patients, as these patients often present with atypical symptoms, or patients with clinically atypical presentations (e.g., PPA), as these are pathologically heterogeneous syndromes that are variably associated with AD pathology (Class III, Level C). Also, below the age of 70 years, frequency of amyloid deposits in controls is low (<20%)
    iii. The differential diagnosis between AD and FTD, because amyloid plaques are not part of the FTLD pathological spectrum (Class III, Level C)
    iv. The differential diagnosis between cerebral amyloid angiopathy (CAA) and intracranial haemorrhage caused by small vessel disease, because patients with CAA but not those with small-vessel disease have positive amyloid imaging scans (Class III, Level C).

Recommendations for Serial Structural MRI

1. Changes over a relatively short period (e.g., 6 months to 1 year) that are visible to the naked eye may strengthen the clinical suspicion of neurodegenerative dementia, particularly in MCI patients (Class IV, Good Practice Point).
2. In most cases, advanced image registration techniques are needed to pick up subtle structural changes over time, but these are restricted to research use or clinical trials (Class IV, Good Practice Point).

Recommendations for Non-conventional MRI

1. At present, advanced MRI techniques do not have a role in the diagnosis or routine assessment or monitoring of neurodegenerative dementia (Class IV, Good Practice Point).
2. The reliability and reproducibility of advanced MRI techniques requires further evaluation, and serious efforts are under way to achieve harmonization of both acquisition and post-processing procedures.

Definitions:

Evidence Classification Scheme for a Diagnostic Measure

Class I: A prospective study in a broad spectrum of persons with the suspected condition, using a 'gold standard' for case definition, where the test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy.

Class II: A prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by 'gold standard') compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy.

Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where test is applied in a blinded evaluation.

Class IV: Any design where test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls).

Rating of Recommendations for a Diagnostic Measure

Level A rating (established as useful/predictive or not useful/predictive) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (established as probably useful/predictive or not useful/predictive) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (established as possibly useful/predictive or not useful/predictive) requires at least two convincing class III studies.

Good Practice Points (GPP) Where there was a lack of evidence, but clear consensus, good practice points are provided.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Alzheimer's Disease (AD)
- Dementia

Guideline Category

Diagnosis

Evaluation

Technology Assessment

Clinical Specialty

Family Practice

Internal Medicine

Neurology

Radiology

Intended Users

Physicians

Guideline Objective(s)

- To revise and expand previous European Federation of Neurological Societies (EFNS) recommendations on the use of structural and functional neuroimaging for the diagnosis and management of patients with Alzheimer's disease (AD)
- To provide an overview of the evidence for the use of neuroimaging techniques in vascular dementia and other neurodegenerative dementias
- To provide general recommendations that apply to all types of dementia in clinical practice

Target Population

Patients with suspected or diagnosed Alzheimer's disease (AD) or dementia

Interventions and Practices Considered

1. Magnetic resonance imaging (MRI) (high-resolution structural volumetric T1-weighted scan, transverse T2-weighted and fluid attenuated inversion recovery [FLAIR] sequences, transverse T2*-gradient echo sequence, diffusion-weighted imaging)
2. Computed tomography (CT)
3. Functional imaging
   - Single positron emission computed tomography (SPECT)
   - Positron emission tomography (PET)
4. Amyloid imaging (not recommended for routine use, but as indicated in select circumstances)

Note: Routine contrast administration in MRI was considered but not recommended.

Major Outcomes Considered

Sensitivity and specificity of diagnostic tests

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The evidence for these guidelines has been identified from searches of MEDLINE and references from relevant articles published in peer-reviewed journals before April 2012. Other published meta-analyses, systematic reviews and evidence-based management guidelines in dementia have also been considered, including the practice parameters from the American Academy of Neurology, the previous recommendations for the diagnosis and management of Alzheimer's Disease (AD) and other disorders associated with dementia from the European Federation of Neurological Societies (EFNS), and the National Institute for Health and Clinical Excellence guideline. Only articles published in English were reviewed.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Evidence Classification Scheme for a Diagnostic Measure

Class I: A prospective study in a broad spectrum of persons with the suspected condition, using a 'gold standard' for case definition, where the test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy.

Class II: A prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by 'gold standard') compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy.

Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where test is applied in a blinded evaluation.

Class IV: Any design where test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls).

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

The task force working group reviewed evidence from original research articles, meta-analyses and systematic reviews, published before April 2012. The evidence was classified (see the "Rating Scheme for the Strength of the Evidence" field) according to the European Federation of the Neurological Societies (EFNS) guidance regulations.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Consensus was reached by circulating drafts of the manuscript to the task force members and by discussing the classification of evidence and recommendations. All members had the opportunity to comment on the recommendations and approved the final version of this document.

Consensus recommendations are given and graded according to the European Federation of Neurological Societies (EFNS) guidance regulations. Where there was lack of evidence but consensus amongst experts was reached, the guideline developers have stated their opinion as 'good practice points' (see the "Rating Scheme for the Strength of the Recommendations" field).

Rating Scheme for the Strength of the Recommendations

Rating of Recommendations for a Diagnostic Measure

Level A rating (established as useful/predictive or not useful/predictive) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (established as probably useful/predictive or not useful/predictive) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (established as possibly useful/predictive or not useful/predictive) requires at least two convincing class III studies.

Good Practice Points (GPP) Where there was a lack of evidence, but clear consensus, good practice points are provided.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Peer Review

Description of Method of Guideline Validation

The guidelines were validated according to the European Federation of Neurological Societies (EFNS) criteria (see the "Availability of Companion Documents" field).

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for selected recommendations (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Accurate diagnosis of Alzheimer's disease (AD) and other dementias

Potential Harms

Not stated

Qualifying Statements

Qualifying Statements

This guideline provides the view of an expert task force appointed by the Scientific Committee of the European Federation of Neurological Societies (EFNS). It represents a peer-reviewed statement of minimum desirable standards for the guidance of practice based on the best available evidence. It is not intended to have legally binding implications in individual cases.

Implementation of the Guideline

Description of Implementation Strategy

The European Federation of Neurological Societies has a mailing list and all guideline papers go to national societies, national ministries of health, World Health Organisation, European Union, and a number of other destinations. Corporate support is recruited to buy large numbers of reprints of the guideline papers and permission is given to sponsoring companies to distribute the guideline papers from their commercial channels, provided there is no advertising attached.

Implementation Tools

Staff Training/Competency Material

> For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Filippi M, Agosta F, Barkhof F, Dubois B, Fox NC, Frisoni GB, Jack CR, Johannsen P, Miller BL, Nestor PJ, Scheltens P, Sorbi S, Teipel S, Thompson PM, Wahlund LO. EFNS task force: the use of neuroimaging in the diagnosis of dementia. Eur J Neurol. 2012 Dec;19(12):e131-40, 1487-501. [307 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Dec

Guideline Developer(s)

European Academy of Neurology - Medical Specialty Society

Source(s) of Funding

Guideline Committee

European Federation of Neurological Societies (EFNS) Task Force on Use of Neuroimaging in the Diagnosis of Dementia

Composition of Group That Authored the Guideline

Task Force Members: M. Filippi, Neuroimaging Research Unit, Division of Neuroscience, Institute of Experimental Neurology, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy; F. Agosta, Neuroimaging Research Unit, Division of Neuroscience, Institute of Experimental Neurology, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy; F. Barkhof, Department of Radiology, VU University Medical Center, Amsterdam, The Netherlands; B. Dubois, Centre de Recherche de l'Institut du Cerveau et de la Moelle Epinière, Université Pierre et Marie Curie, Paris, France; N. C. Fox, Dementia Research Centre, Institute of Neurology, University College London, London, UK; G. B. Frisoni, IRCCS Istituto Centro San Giovanni di Dio Fatebenefratelli di Brescia, Brescia, Italy; C. R. Jack, Department of Radiology, Mayo Clinic and Foundation, Rochester, MN, USA; P. Johannsen, Memory Clinic, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark; B. L. Miller, Memory and Aging Center, University of California, San Francisco, CA, USA; P. J. Nestor, Department of Clinical Neuroscience, University of Cambridge, Cambridge, UK; P. Scheltens, Department of Neurology and Alzheimer Center, VU University Medical Center, Amsterdam, The Netherlands; S. Sorbi, Department of Neurological and Psychiatric Sciences, Azienda Ospedaliero-Universitaria di Careggi, Florence, Italy; S. Teipel, Department of Psychiatry, University of Rostock, and German Center for Neuro-degenerative Diseases (DZNE), Rostock, Germany; P. M. Thompson, Department of Neurology, David Geffen School of Medicine at the University of California Los Angeles, Los Angeles, CA, USA; and L.-O. Wahlund, Division of Clinical Geriatrics, Department of Neurobiology, Karolinska Institute, Stockholm, Sweden

Financial Disclosures/Conflicts of Interest

The authors declare no other conflict of interests. General financial interests are listed below:

Massimo Filippi received personal compensation for board membership from Teva Pharmaceutical Industries Ltd., and Genmab A/S; for consultancies from Bayer Schering Pharma, Biogen-Dompé, Genmab A/S, Merck Serono, Pepgen Corporation and Teva Pharmaceutical Industries Ltd.; funding for travel from Bayer Schering Pharma, Biogen-Dompé, Genmab A/S, Merck Serono and Teva Pharmaceutical Industries Ltd.; speakers' bureaus from Bayer Schering Pharma, Biogen-Dompé, Genmab A/S, Merck Serono and Teva Pharmaceutical Industries Ltd. His institution has received grants from Bayer Schering, Biogen-Dompé, Genmab A/S, Merck Serono, Teva Pharmaceutical Industries Ltd., and

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available to registered users from the European Federation of Neurological Societies Web site _____.

Availability of Companion Documents

The following are available:

- Brainin M, Barnes M, Baron JC, Gilhus NE, Hughes R, Selmaj K, Waldemar G; Guideline Standards Subcommittee of the EFNS Scientific Committee. Guidance for the preparation of neurological management guidelines by EFNS scientific task forces – revised recommendations 2004. Eur J Neurol. 2004 Sep;11(9):577-81. Electronic copies: Available in Portable Document Format (PDF) from the European Federation of Neurological Societies Web site _____.
- Continuing Medical Education questions are available to registered users from the European Journal of Neurology Web site _____.

Patient Resources

None available

NGC Status

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